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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/864,866	05/23/2001	R. Stephen Lloyd	268.001^0101	2264

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EXAMINER	
WALICKA, MALGORZATA A	

ART UNIT	PAPER NUMBER
2652	19

DATE MAILED: 04/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/864,866	LLOYD ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)[·] Responsive to communication(s) filed on *28 January 2003* .

2a)[·] This action is **FINAL**. 2b)[ ] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *1-441* is/are pending in the application.

4a) Of the above claim(s) *21-40* is/are withdrawn from consideration.

5)[ ] Claim(s) _____ is/are allowed.

6)[·] Claim(s) *1-4,9-12 and 41-44* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[·] The specification is objected to by the Examiner.

10)[ ] The drawing(s) filed on _____ is/are: a)[ ] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) [ ] Interview Summary (PTO-413) Paper No(s). _____ .
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: .

The Amendment and Response filed on January 28, 2003 as paper No.18 is acknowledged. The amendments to the specification and claims have been entered as requested. Claims 1-4, 9-12 and 21-40 are amended. Claims 1-4, 9-12 and 21-44 are pending in the application. Claims 1-4, 9-12 and 41-44 are the subject of this Office Action. Claims 21-40 are withdrawn from consideration as drawn to the nonelected invention.

Detailed Action

1. Request for Rejoinder under 37 CFR § 1.121

The request for rejoinder of claims 21-40 withdrawn from consideration as a result of restriction requirement has been noted. The issue will be addressed when the product of the elected claims 1-4, 9-12 and 41-44 will be found patentable.

2. Rejection under 35 USC section 112, first paragraph.

2.1. Lack of written description

The rejection of claims 1-4, 11-12 and 43-44 made under this paragraph in the previous Office Actions is withdrawn because the claims have been amended.

2.2. Scope of enablement

Rejection of claims 1-4, 11-12 and 43-44 made under 35 U.S.C. 112, first paragraph made in the previous Office Action paper No. 16 and 11 is not withdrawn for the reason of record that are reiterated here bellow.

The claims are rejected because the specification, while being enabling for polypeptides having glycosylase activity and sequence selected from the group consisting of SEQ ID NO: 41, 42 and 43 does not reasonably provide enablement for any pyrimidine glycosylase or a pyrimidine glycosylase/AP lyase that is at least 60% identical to SEQ ID NO: 41, 42 or 43.

The Applicants argue the question of enablement in the section concerning written description. Particularly, Applicants argue, "detailed instructions **for making** [emphasis MW] polypeptides with an amino acid sequence having at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO: 41, SEQ ID NO: 42, and SEQ ID NO: 43. See p.11, line 15 - p.12, line 16 of the specification. Likewise, the specification provides complete information for making polypeptides with the claimed functional characteristics, having pyrimidine glycosylase or pyrimidine glycosylase/AP lyase activity. See, for example, p. 8, lines 14 - 24; p. 9, line 19 - p. 10, line 26; p. 43, line 24 - p. 44, line 22; and page 52, line 17 – p. 53, line 15 of the specification." This argument has been found not persuasive in the previous Office Action and remains not persuasive, for the reasons explained bellow.

As indicated in the previous Office Action, the instructions given on quoted pages and lines are as follows.

(a) p.11, line 15 - p.12, line 16

"The present invention further includes polypeptides having pyrimidine glycosylase activity, preferably pyrimidine glycosylase/AP lyase activity, and amino acid identity with the amino acid sequence of SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43, preferably SEQ ID NO: 41 or SEQ ID NO: 42. Amino acid identity is defined in the context of a comparison between a polypeptide and SEQ

ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43, and is determined by aligning the residues of the two amino acid sequences (i.e., a candidate amino acid sequence and the amino acid sequence of SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43) to optimize the number of identical amino acids along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids, although the amino acids in each sequence must nonetheless remain in their proper order. A candidate amino acid sequence is the amino acid sequence being compared to an amino acid sequence present in SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43. A candidate amino acid sequence can be isolated from a microbe or a microbe harboring a virus, or can be produced using recombinant techniques, or chemically or enzymatically synthesized. Preferably, two amino acid sequences (i.e., the candidate amino acid sequence and the amino acid sequence present in SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43) are compared using the Blast program of the BLAST2 search algorithm, as described by Tatusova, et al. (*FEMS Microbiol Lett* 1999, 174:247-250), and available at www.ncbi.nlm.nih.gov/gorf/b12.html. Preferably the default values, for all Blast 2 search parameters are used, including matrix=BLOSUM62; open gap penalty =11, extension gap penalty =1, gap x_dropoff=50, expect=10, wordsize=3, and filter on. In comparison of two amino acid sequences using the Blast search algorithm, amino acid identity is referred to as "identities." Preferably, a polypeptide having pyridine glycosylase activity has an amino acid

sequence having in increasing order of preference, at least about 15% amino acid identity, at least about 30% amino acid identity, at least about 40% amino acid identity, at least about 50% amino acid identity and most preferably, at least 60% amino acid identity to SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43."

Fragment (a) quoted as the first by Applicants instructs how to align sequences and not how to make a sequence having glycosylase or glycosylase/AP lyase activity and at least about 60% identity to any of the SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43.

(b) p. 8, lines 14-24

"As used herein, 'pyrimidine glycosylase' refers to a polypeptide that recognizes the presence of two consecutive damaged bases in a polynucleotide and catalyzes the breakage of the glycosyl bond between the 5' base and the DNA sugar-phosphate backbone. A polypetide that recognizes the presence of two consecutive damaged pyrimidine bases and catalyzes the breakage of such a bond has 'glycosylase activity.' Whether a polypeptide has pyrimidine glycosylase activity can be determined by measuring the ability of the polypeptide to cleave the glycosyl bond of the 5' pyrimidine of a cyclobutane pyrimidine dimer in DNA. Such methods are known to the art. A polypeptide having pyrimidine glycosylase activity is often referred to in the art as a pyrimidine dimmer-specific DNA glycosylase."

The above quoted fragment (b) defines the glycosylase activity and suggests how to examine the presence of this activity for a particular protein. The passage, however, does not instruct how to make an amino acid sequence having glycosylase or glycosylase/AP lyase activity and at least about 60% identity to any of the SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43.

(c) p. 9, line 19 - p. 10, line 26

Optionally and preferably, a polypeptide of the present invention also has apurinic/apirymidinic lyase activity (AP lyase activity). A polypeptide having pyrimidine glycosylase activity and AP activity is referred to herein as a 'pyrimidine glycosylase/AP lyase,' and has 'pyrimidine glycosylase/AP lyase activity.' Thus, a preferred polypeptide of the present invention has pyrimidine glycosylase/AP lyase activity and a targeting sequence, preferably an exogenous targeting sequence. As used herein, 'AP lyase activity' refers to the ability of a polypeptide to catalyse a β-elimination reaction on an abasic site containing DNA, resulting in an α, β unsaturated aldehyde. A polypeptide having pyrimidine glycosylase/AP lyase activity is often referred to in the art as a 'pyrimidine dimmer specific DNA glycosylase/AP lyase.'

Whether a polypeptide has pyrimidine glycosylase/AP lyase activity can be determined by measuring the ability of the polypeptide to incise a target polynucleotide containing damaged bases in the presence of a buffer. The target

polynucleotide contains damaged bases, preferably, UV radiation induced pyridine dimmers. An example of a target polynucleotide is disclosed in the Examples. Preferably, the target polynucleotide is present at a concentration of from about 0.1 nM to about 10 nM. The putative glycosylase/AP lyase is present at concentration of from about 0.1 nM to about 100 nM...' quotation not finished for brevity's sake.

The above quoted specification fragment defines specifically apurinic/apirymidinic lyase activity (AP lyase activity) and the name glycosylase/AP lyase. Further, the passage describes conditions, under which the glycosylase/AP lyase assay may be performed. The passage, however, does not instruct how to make an amino acid sequence having glycosylase or glycosylas/AP lyase activity and at least about 60% identity to any of the SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43.

(d) p. 43, line 24 - p. 44, line 22;

This passage from the specification is part C. *Enzymatic activity* of Example I, and describes enzymatic assay of the purified enzymes containing the mitochondrial localization signal. Thus, the text on p. 43, line 24 – p. 44, line 22 does not instruct how to make an amino acid sequence having glycosylase or glycosylase/AP lyase activity and at least about 60% identity to any of the SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43.

(e) page 52, line 17 – p. 53, line 15

The passage teaches plasmid nicking assay of recombinant enzymes containing

nuclear localization signal. Again, this is an assay for determination of enzymatic activity of a polypeptide, and not an instruction how to make an amino acid sequence having glycosylase or glycosylase/AP lyase activity and at least about 60% identity to any of the SEQ ID NO: 41, SEQ ID NO: 42, or SEQ ID NO: 43.

In summary, the passages to which Applicants refer the examiner provide instruction for making alignment of amino acid sequences, define the enzyme activities and describe methods of measurement of said activities.

Applicants assert that they provided description of making the claimed inventions in the fragments of the specification enumerated as (a)-(e) above. Applicants' arguments have been fully considered but are found not persuasive because none of the fragments of the specification that Applicants refer to is providing written descripton of how to make the polypeptides having pyrimidine glycosylase or a pyrimidine glycosylase/AP lyase activity and having at least 60% identity to SEQ ID NO: 41, 42 or 43.

One skilled in the art concludes that the specification does not contain written description of the invention, and of the manner and process of making it, in such full, and exact terms as to enable any person skilled in the art to make and use the same.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

Rebecca Prunty

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